Q fever is endemic in Northern Ireland, with incidence levels only second to south western England in the United Kingdom. The incidence of Q fever peaks in April to May, which can probably be in part be explained by the calving and lambing season.[2] In Northern Ireland there were six deaths between 1962 and 1989 attributable to Q fever.[5] These deaths were due to cardiac complications and one suicide. Q fever can be thought of as an occupational hazard, affecting farmers, abattoir workers, and veterinarians. However the organisms can survive for long periods in the environment, so the population as a whole is at risk. There were no occupational risk factors in this case.

Q fever is a treatable disease, with tetracyclines being the antibiotics of choice.[1] Our patient was treated initially with a two week course of oxytetracyline 500 mg four times a day, and subsequently re-treated with a further four week course in view of ongoing night sweats. He remained well at six month follow up with no significant symptoms and mildly cholestatic liver enzymes.

As our case demonstrates Q fever may cause acute hepatitis and acute liver decompensation. The diagnosis should always be considered in patients with an unexplained pyrexia and hepatitis, especially in endemic regions.

Final diagnosis

Q fever.

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A young man with weight loss and depression

Q1: What is the clinical diagnosis?

The clinical diagnosis is Cushing's syndrome. The presence of thin atrophic skin, facial plethora, hyperpigmentation over the knuckles, proximal myopathy, hypokalaemia, psychiatric symptoms, hypertension, and diabetes mellitus led to the diagnosis of Cushing's syndrome in this patient.

Q2: How should this patient be investigated?

The basal cortisol levels were raised with loss of diurnal rhythm (am: 1200 nmol/l, pm: 1200 nmol/l). The diagnosis of Cushing's syndrome was confirmed by non-suppressible serum cortisol (1200 nmol/l) with low dose dexamethasone challenge (0.5 mg every six hours for 48 hours). High evening cortisol with very inappropriately raised plasma adrenocorticotrophin (ACTH) levels (79 pmol/l) and non-suppressible serum cortisol (1200 nmol/l) with high dose dexamethasone challenge (2 mg every six hours for 48 hours) raised the possibility of an ectopic source of ACTH. Magnetic resonance imaging of the sella was done and was normal. Subsequently computed tomography of the chest and abdomen were performed. Computed tomography of the chest revealed an anterior mediastinal mass (fig 1). Computed tomography of the abdomen showed bilateral adrenal hyperplasia (fig 2). Urinary 5-hydroxyindole acetic acid was negative.

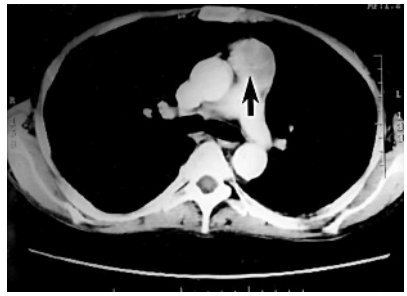

Figure 1 Contrast enhanced computed tomogram of chest showing a well circumscribed mass in the anterior mediastinum.

Q3: What are the treatment modalities available?

The treatment of choice in this patient is resection of the tumour. The tumour was found to be a thymic carcinoid on histopathological examination. Preoperatively the patient was treated with ketaconazole (1200 mg/day) and spironolactone (100 mg/day) with reduction in the dosage of antihypertensives and normalisation of serum potassium levels. After surgical resection of the tumour, the patient was able to stop taking antihypertensives and insulin and his psychiatric symptoms had abated; there was a gain in weight of 4 kg after six weeks of follow up.

Discussion

Cushing's syndrome is the result of chronic glucocorticoid excess either from endogenous hypersecretion or from exogenous therapy. The latter is the most common cause of Cushing's syndrome in clinical practice. Patients with Cushing's syndrome classically present with centripetal obesity, which is seen in 90% of the cases. Though weight gain is the rule in Cushing's syndrome, a paradoxical weight loss can be seen in a subgroup of patients, including those with a malignant tumour as the cause of Cushing's syndrome.[1] Other causes of weight loss in Cushing's syndrome are shown in box 1. Depression, uncontrolled diabetes, and the tumour itself could all have contributed to weight loss in our patient. Other manifestations of Cushing's syndrome include thin atrophic skin with easy bruisability, violaceous striae, proximal muscle weakness, hirsutism, acne, plethora, hypertension, and impaired glucose tolerance. Our patient did not have striae and easy bruisability but had severe proximal myopathy, thin atrophic skin, hypertension, and diabetes.

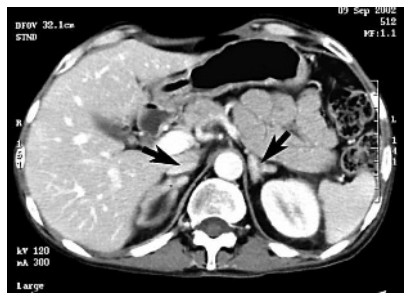

Figure 2 Contrast enhanced computed tomogram of abdomen showing bilateral adrenal hyperplasia.

Box 1: Causes of weight loss in Cushing's syndrome

- Adrenocortical carcinoma.
- Ectopic ACTH secreting tumours (small cell carcinoma of lung).
- Uncontrolled diabetes mellitus.
- Opportunistic infections (tuberculosis, systemic fungal infections).
- Severe depression.
- Associated thyrotoxicosis (McCune-Albright syndrome).

Box 2: Causes of ectopic Cushing's syndrome

- Small cell carcinoma of the lung.
- Bronchial carcinoid.
- Medullary carcinoma of the thyroid.
- Thymic carcinoid.
- Islet cell tumours.
- Pheochromocytoma.
- Ovarian tumours.

Ectopic Cushing's syndrome is seen in 15% to 20% of patients and lung tumours, including small cell carcinoma and bronchial carcinoids, account for 50% of these cases. In contrast to Cushing's disease, which has a female preponderance, ectopic Cushing's syndrome affects both sexes equally. Patients with small cell carcinoma of the lung and thymic carcinoid have a slight male preponderance.[1] Several tumours have been associated with the ectopic production of ACTH resulting in Cushing's syndrome and less commonly corticotrophin releasing hormone (box 2).

Hypokalaemic alkalosis is seen in about 15% of patients with Cushing's syndrome, particularly in those with ectopic Cushing's syndrome. Patients with ectopic Cushing's syndrome often do not have the classical clinical features of the disease. Hyperpigmentation, hypokalaemic alkalosis, and anorexia with weight loss are often seen in these patients, as in our patient.[2] This probably reflects the rapidity of the clinical course rather than atypical presentation.

Thymic carcinoid accounts for 5% to 10% of cases with ectopic Cushing's syndrome.[3] Thymic carcinoids arise from the amine precursor uptake and decarboxylation cells which can secrete a variety of peptide hormones including ACTH and corticotrophin releasing hormone. Carcinoid tumours arising from the embryonic foregut, including thymus, are deficient in the enzyme L-amino

acid decarboxylase. Therefore they have less serotonin secreting capacity and have a greater tendency for peptide hormone production. Our patient did not have the manifestation of serotonin hypersecretion and had very high ACTH levels. The clinical severity of the endocrine disease is related to the size of the tumour. The appearance of the tumour can precede, follow, or occur simultaneously with the manifestations of Cushing's syndrome.[4] As the thymic carcinoids are slow growing tumours, they may clinically and biochemically mimic pituitary Cushing's disease.[5] Up to one third of patients with thymic and bronchial carcinoids have suppressible serum cortisol with high dose dexamethasone compared with 10% of patients with other causes of Cushing's syndrome.

Surgical resection of the tumour is curative in most of the cases with thymic carcinoid. However some advocate radiotherapy postoperatively to prevent recurrence. Thymic carcinoids have varying biological behaviour with the clinical course closely related to the histological differentiation. Moran *et al* reported a five year disease-free survival of 50%, 20%, and 0% in well differentiated, moderately differentiated, and poorly differentiated tumours respectively.[6]

Final diagnosis

Ectopic Cushing's syndrome due to thymic carcinoid.

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